AMENDMENT

In the Specification

Please amend the Specification as follows:

Please delete the title on page 1, lines 12-13 "THERAPEUTIC ANTIANGIOGENIC COMPOSITIONS AND METHOD OF USE" and insert therefor the new title --ENDOSTATIN PROTEIN AND FRAGMENTS THEREOF--.

Page 1, line 15, please insert the following: --This invention may have been made in part by funds from NIH grants RO1-CA64481 and PO1-CA45548. The U.S. government may have certain rights in this invention.--

Page 1, line 16, following "This application" and prior to "claims priority" please insert --is a continuation application of U.S. Patent Application Serial No. 09/154,302, filed September 16, 1998, which is a divisional application of U.S. Patent Application Serial No. 08/740,168, filed October 22, 1996 and issued as U.S. Patent No. 5,854,205, which--.

Page 2, line 27, following "plasminogen" please insert --. --.

Page 4, line 11, please delete "disease" and insert therefor -- diseases--.

Page 10, line 7, please delete "are" and insert therefor --were--.

Page 11, line 14, please delete "substatnial" and insert therefor -- substantial--.

Page 12, line 12, please delete "labelling" and insert therefor --labeling--.

Page 12, line 15, please delete "Labelling" and insert therefor --Labeling--.

Page 12, line 19, please delete "seqence" and insert therefor --sequence--.

Page 14, line 21, please delete "then" and insert therefor --them--.

Page 15, line 18, following "of incubation" please insert --,--.

Page 18, line 14, please delete "occured" and insert therefor —occurred--.

Page 18, line 15, please delete "possible" and insert therefor —possibly--.

Page 21, line 15, please delete ", ," and replace therefor --,--.

Page 24, line 34, following "metastases" please insert --.--.

Page 30, line 28, after "antigen." Please insert -- -- before "The".

Page 31, line 15, please delete "tisssue" and insert therefor --tissue--.

Page 36, line 19, please delete "examles" and insert therefore --examples--.

Page 38, line 22, following "MARRASVGTD" please insert --SEQ ID NO:2--.

Page 38, line 22, following "RRAS" please insert --SEQ ID NO:3--.

Page 40, line 22, please delete "recombinanty" and insert therefore --recombinantly--.

Page 43, line 21, delete "." and replace therefor --,--.

Page 45, line 25, please delete "approximatley" and insert therefor --approximately--.

Page 45, line 31, please delete "deetermining" and insert therefor --determining--.

Page 47, line 1, please delete "analysed" and insert therefor --analyzed--.

Page 47, line 28, please delete "analysed" and insert therefor --analyzed--.

Page 47, line 30, please delete "analysed" and insert therefor --analyzed--.

Page 48, line 30, please delete "?" and insert therefor --.--.

Pages 55 and 56, please replace the Sequence Listing with the enclosed replacement pages numbered 55-56 which contain the substitute Sequence Listing.

Replacement pages 55 and 56 are submitted in conjunction with the Transmittal of Sequence Listing enclosed herewith.

Please delete the Brief Description of Figure 7 on page 8, line 31, through page 9, line 12, and replace therefor:

--Figure 7A-C: *Systemic Therapy with Recombinant Endostatin Regresses Lewis Lung Carcinoma Primary Tumors.*

Figure 7A. Mice were implanted subcutaneously on the dorsum with Lewis lung carcinoma cells. Systemic therapy with recombinant mouse endostatin (20 mg/kg/day) demonstrated that endostatin inhibitor inhibited tumors by >99% relative to saline-treated controls. Each point represents mean ± SEM for 5 mice. The experiment was repeated with comparable results.

Figure 7B. Representative treated and untreated tumor-bearing mice after 11 days of systemic therapy with endostatin. Saline-treated mice (right) had rapidly growing red tumors with ulcerated surfaces. Endostatin treated mice (left) had small pale residual tumors (arrow).

Figure 7C. Residual disease in endostatin treated mice. Three of the five endostatin treated mice were sacrificed after 16 days of therapy. Autopsy revealed small white residual tumors at the site of the original primary implantation (arrows).--

Please delete the Brief Description of Figure 12 on page 10, lines 11 through 23, and replace therefor:

--Figure 12A-C: *Endostatin Results in an Inhibition of Angiogenesis and an Increase in Apoptosis of Lewis Lung Carcinoma Primary Tumors.*

Histological sections of tumors from saline versus endostatin treated mice implanted with Lewis lung carcinomas were analyzed for proliferation (PCNA), apoptosis (TUNEL), and angiogenesis (vWF). There was no significant difference in the proliferative index of tumor cells (Figure 12A) in treated versus untreated tumors. In contrast, the apoptotic index of the tumor cells (Figure 12B) increased 8-fold ($p < 0.001$) in the endostatin treated mice. Vessel density (Figure 12C) was determined by counting the number of capillary blood vessels per high-power field (HPF) in sections stained with antibodies against vWF. Angiogenesis was almost completely suppressed in the residual microscopic tumors of the endostatin treated mice ($p < 0.001$).--

On page 63, lines 5-9, please delete the current Abstract and insert the following new Abstract, a separate copy of which is attached hereto:

-- ENDOSTATIN PROTEIN AND FRAGMENTS THEREOF

Abstract of the Invention

The present invention provides anti-angiogenic compositions, and more particularly provides endostatin protein fragments. The compositions of the present invention may be used for the treatment of angiogenesis-dependent diseases such as cancer.--

In the Claims

Please amend the claims as follows:

Please cancel claims 1 through 33.

Please add the following new claims:

--34.(New) An isolated endostatin protein comprising, an amino acid sequence of a fragment of a C-terminal region of a collagen protein, wherein the endostatin